

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE APPLICATION OF

Art Unit: 1647

NICO CERLETTI

Examiner: D. Romeo

APPLICATION NO: Not Yet Assigned

FILED: Herewith

FOR: NEW PROCESS FOR THE PRODUCTION OF BIOLOGICALLY ACTIVE PROTEIN

Assistant Commissioner for Patents  
Washington, D.C. 20231

PRELIMINARY AMENDMENT

Sir:

Kindly enter the following preliminary amendment prior to calculating the filing fee for the application.

IN THE SPECIFICATION

At page 1, between lines 1 and 2, insert--This is a continuation of U.S. Application No. 09/316,724, filed 5/21/99, which is a continuation of U.S. Application No. 08/776,444, filed 1/24/97 (now abandoned).

IN THE CLAIMS

Delete claims 1-18. Add the following claims 19-25.

19. Process for the production of a dimeric, biologically active Transforming Growth Factor type  $\beta$ 2 (TGF- $\beta$ 2) or  $\beta$ 3 (TGF- $\beta$ 3), or a salt thereof, comprising treating the denatured monomeric form of said TGF- $\beta$ 2 or  $\beta$ 3 with a folding buffer comprising an organic solvent selected from the group consisting of DMSO (Dimethylsulfoxide), and DMF (Dimethylformamide) and a mixture thereof, said buffer additionally containing glutathione in its reduced form; thereby permitting folding of the monomeric TGF- $\beta$ 2 or  $\beta$ 3 into the spatial conformation which after dimerization is associated with the biological activity, while retaining said monomer in a soluble form; the process being conducted in the substantial absence of either a chaotropic agent or a copper or manganese salt.

20. The process according to claim 54 in which DMSO is used at a concentration of about 30% to about 50% (vol/vol).

21. The process according to claim 54 in which DMF is used at a concentration of 40% (vol/vol).

22. The process according to claim 54 wherein the organic solvent is a mixture of DMSO and DMF and the mixture is used in a concentration of 10% to about 50%(vol/vol).

23. The process according to claim 54 in which the buffer has a pH of about 8.5 to about 10.

24. The process according to claim 54 in which the buffer has a temperature of about 0°C to about 40°C.

25. The process according to claim 54 in which the reduced glutathione is used in a concentration of about 1 mM to 100 mM.

REMARKS

Early examination of the claims and allowance of the same are respectfully requested.

Respectfully submitted,

  
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